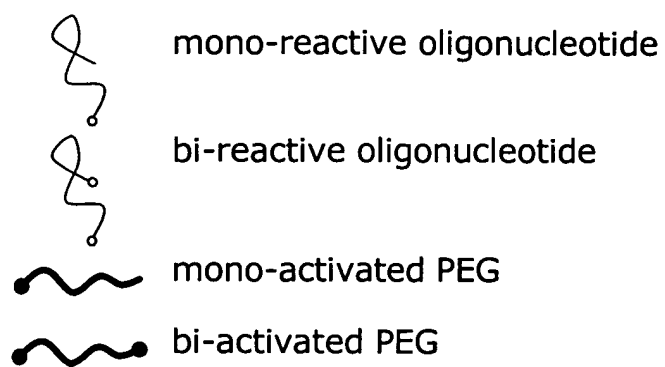
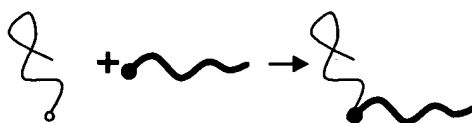


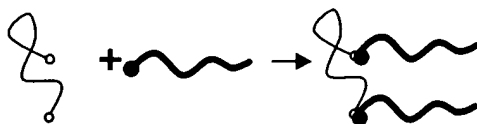
Figure 1



standard PEGylation



multiple PEGylation



dimerization via PEGylation

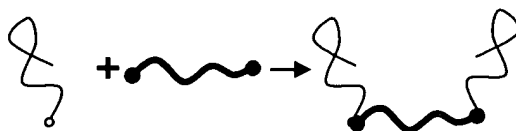
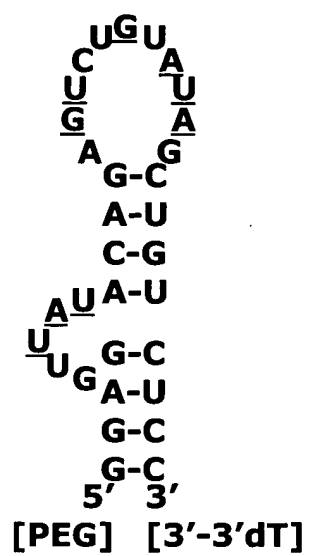


Figure 2

(A).



SEQ ID NO:151

(B)

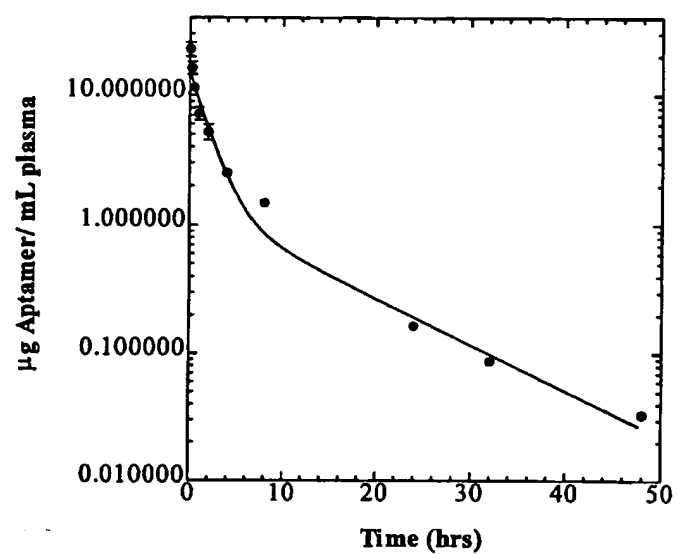


Figure 3

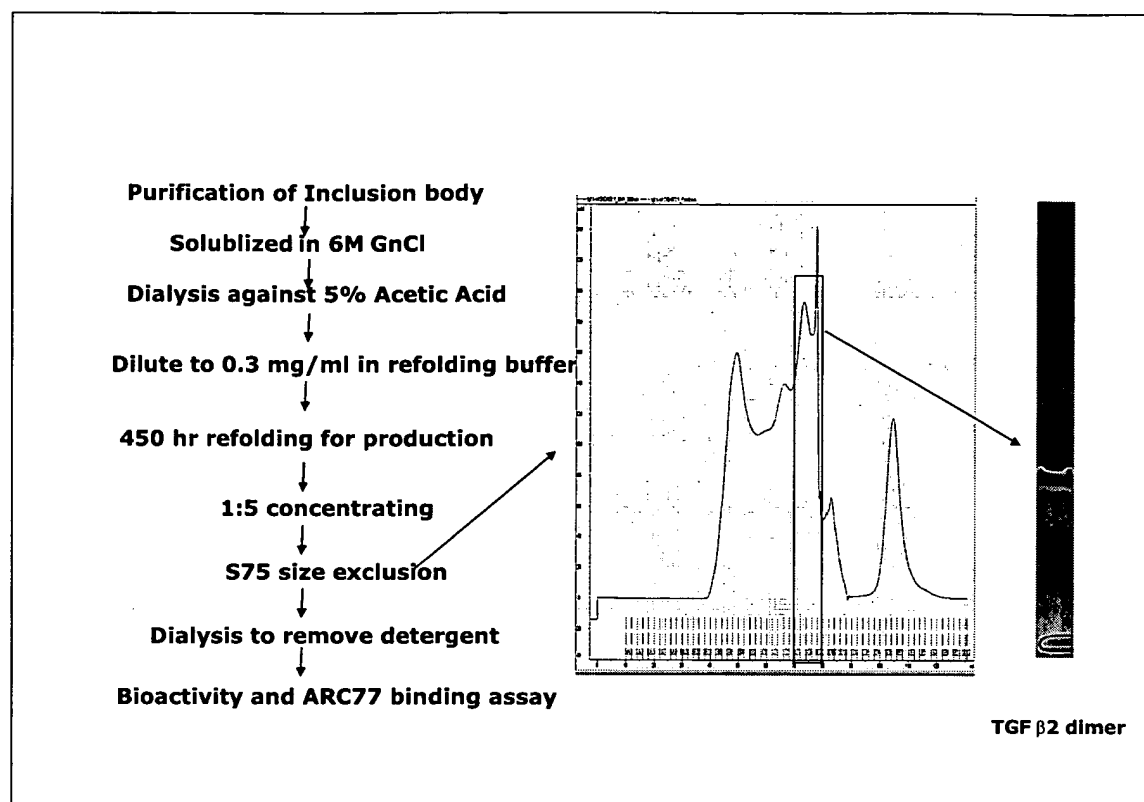


Figure 4

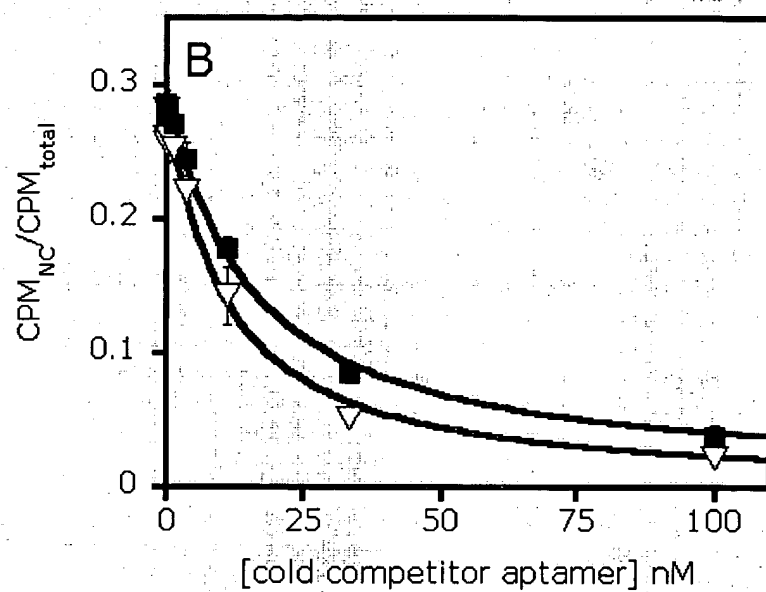
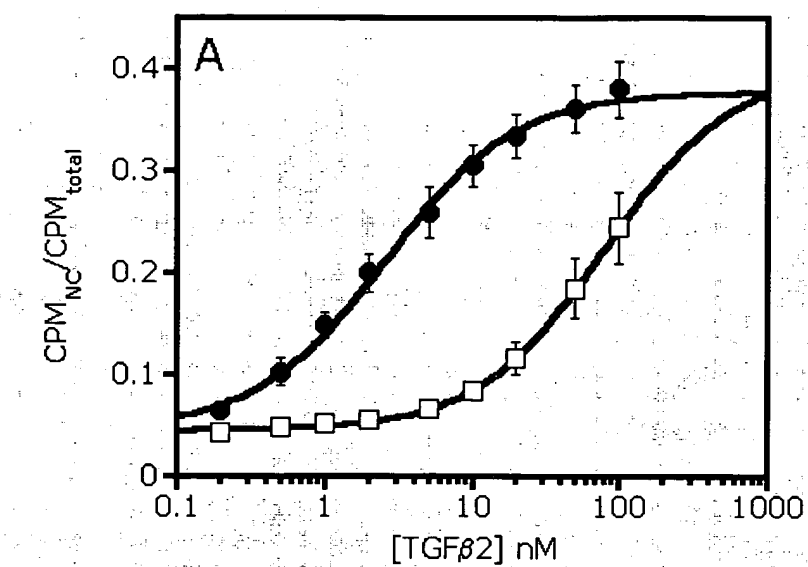
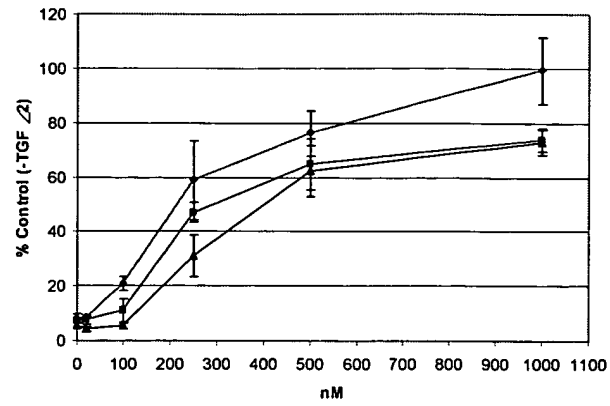
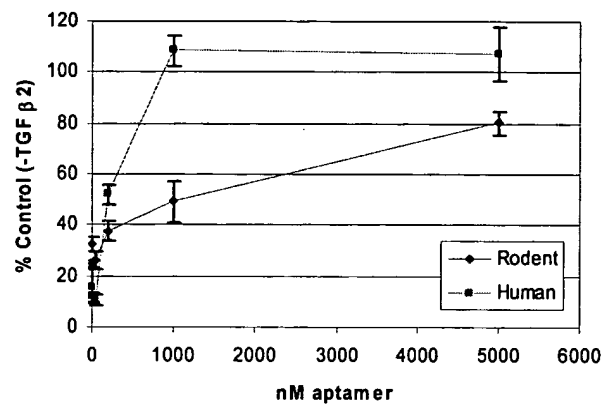


Figure 5

A.



B.



C.

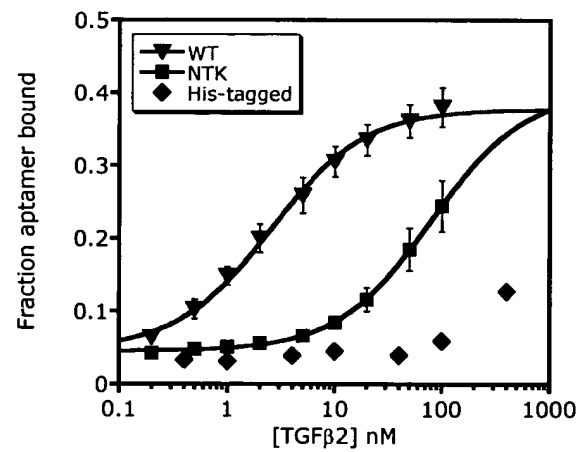
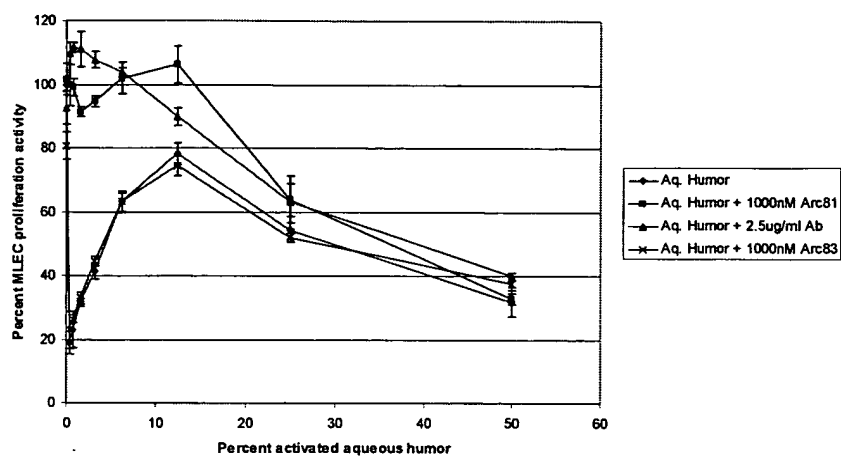
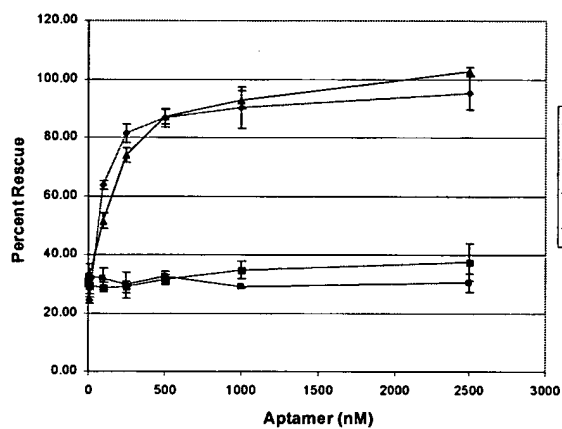


Figure 6

A.



B.



C.

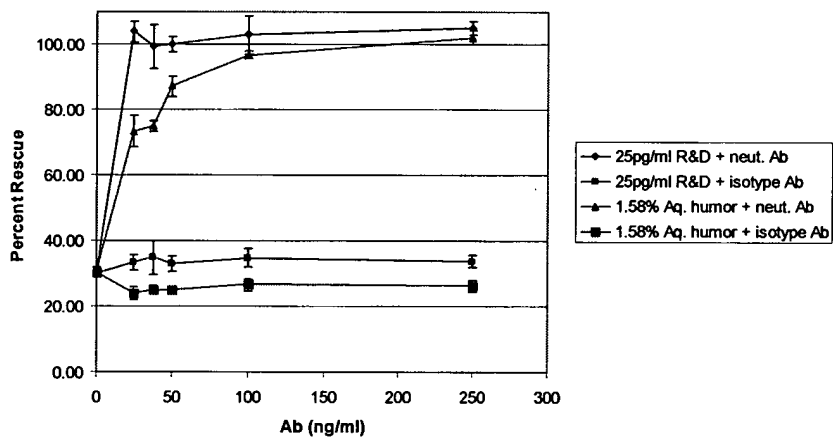


Figure 7

Selection, minimization and characterization of a TGF β 2 aptamer

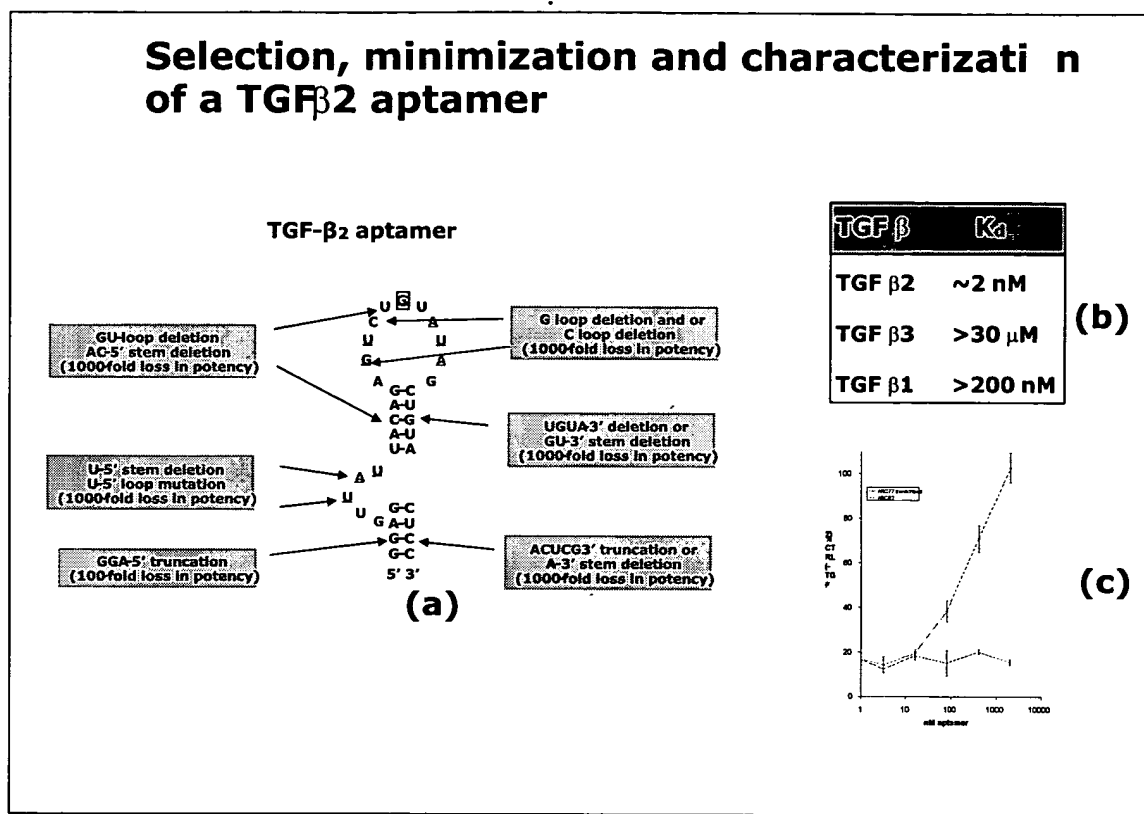


Figure 8

Alpha-screen assay suggests 2:1 aptamer/TGF β 2 stoichiometry

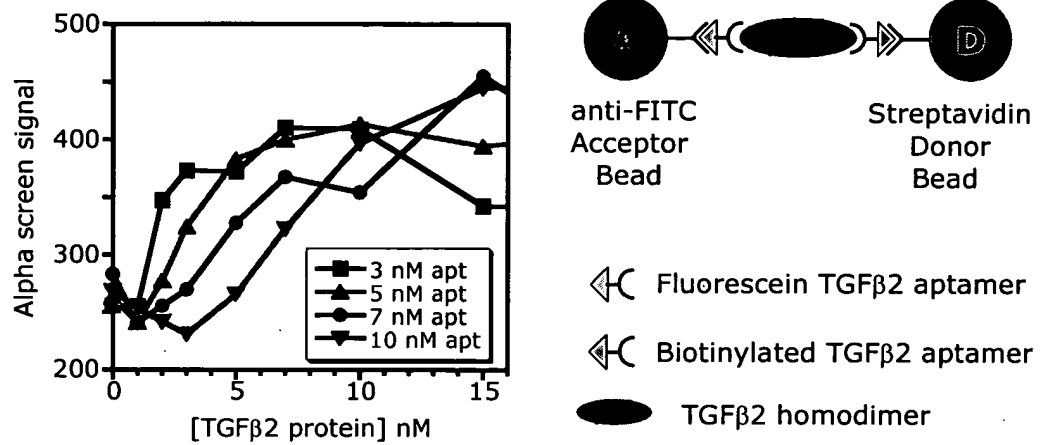


Figure 9

Modifications of TGF b2 have different effects on its activity and aptamer binding affinity

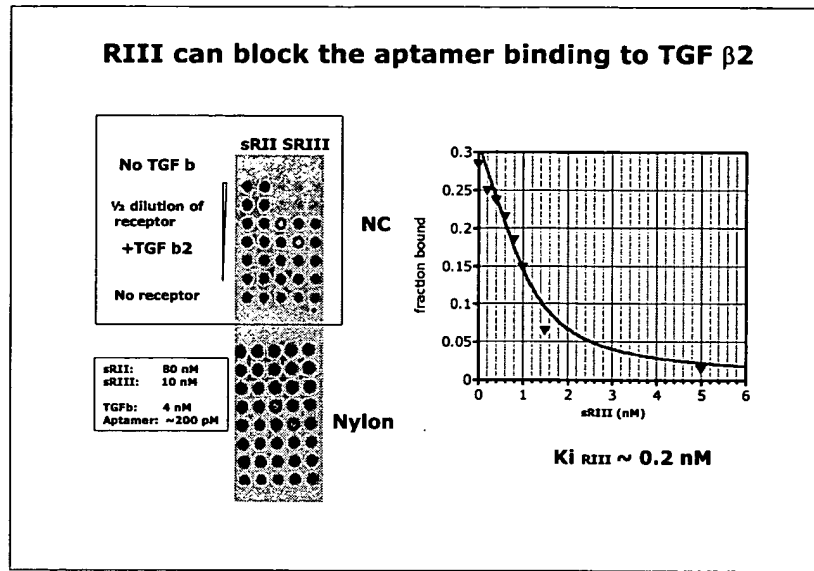
WT ALDAAYCFRNVQDNCCLRPLYIDFKRDLGW ((SEQ ID NO: 152))
N-Long tag MRGSHHHHHHGMASMTGGQMQMRDLYDDDDKDRWALDAAYCFRNVQDNCCLRPLYIDFKRDLGW ((SEQ ID NO: 153))
N-short tag MHHHHHALDAAYCFRNVQDNCCLRPLYIDFKRDLGW ((SEQ ID NO: 154))

WT GYNANFCAGACPYLW SSDTQHSRVLSLYNTINPEASAPCCVSQDLEPLTILYYIGKTPKIEQ LSNMI ((SEQ ID NO: 155))
N-Long tag GYNANFCAGACPYLW SSDTQHSRVLSLYNTINPEASAPCCVSQDLEPLTILYYIGKTPKIEQ LSNMI ((SEQ ID NO: 156))
N-short tag GYNANFCAGACPYLW SSDTQHSRVLSLYNTINPEASAPCCVSQDLEPLTILYYIGKTPKIEQ LSNMI ((SEQ ID NO: 157))

TGF b2	EG100 (pM)	Kd aptamer (nM)	Ic50 aptamer (nM)
WT	~0.5	~2.5	~200
S59T/R60K/K94N	~0.5	~80	~3000
K94N	~0.5	~2.5	~200
N-long tag	~40	>500	No effect
N-short tag	~20	~300	n.d.

Figure 10

A.



B.

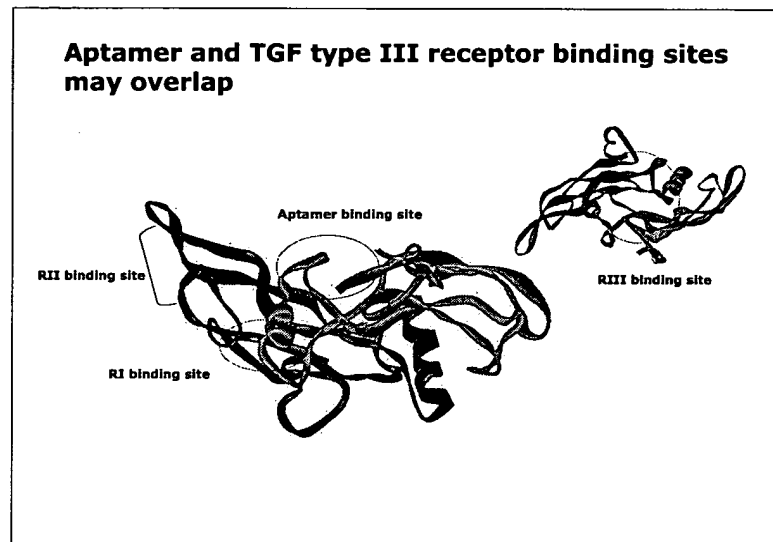


Figure 11

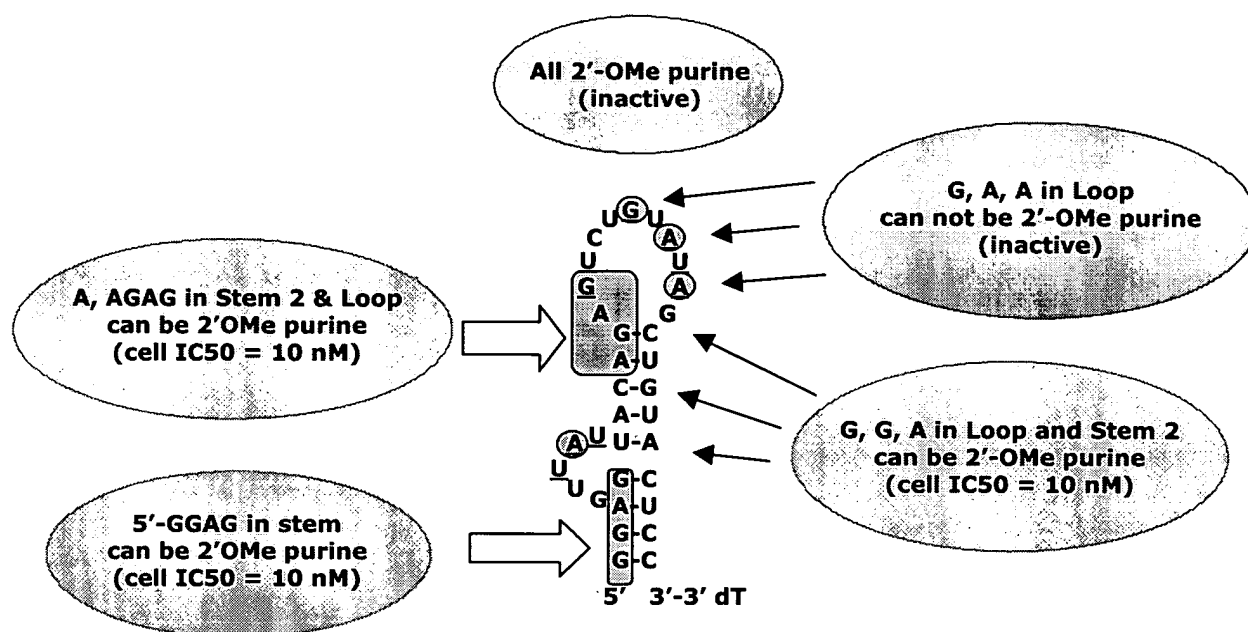
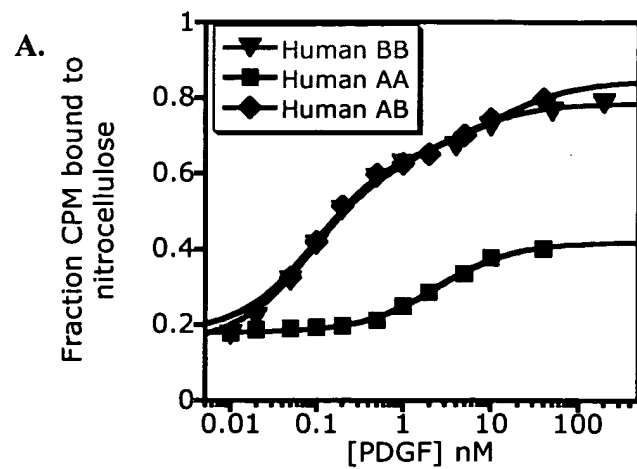
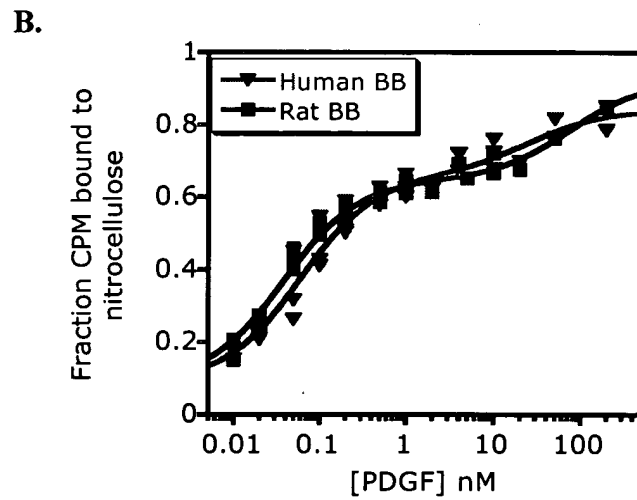


Figure 12



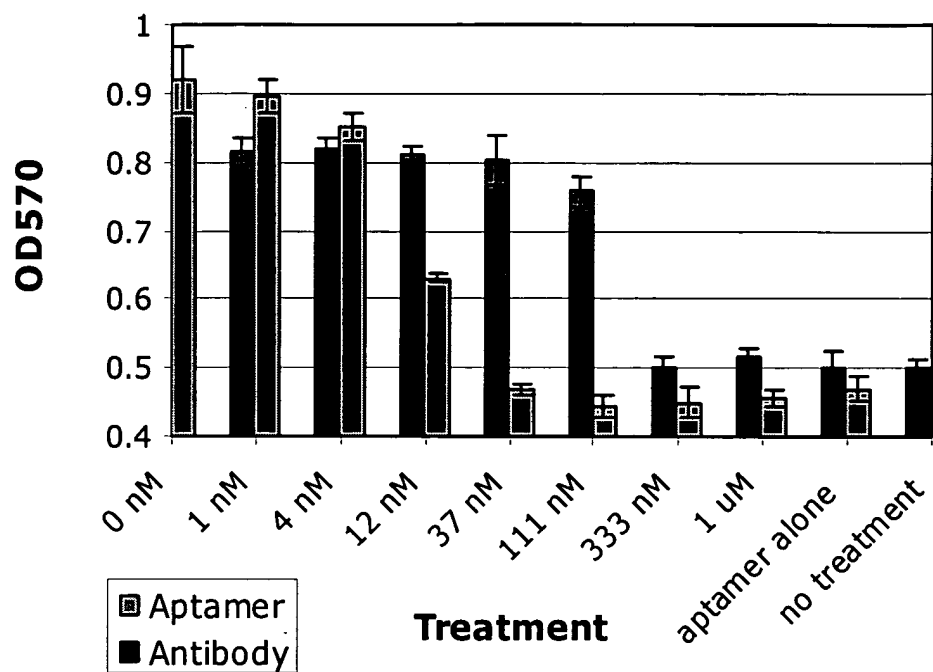
Protein	K_{D1} (nM)	K_{D2} (nM)
BB	0.09 ± 0.02	~ 5
AA	n.d.	2.6 ± 0.2
AB	0.10 ± 0.01	~ 15



Protein	K_{D1} (nM)	K_{D2} (nM)
Human	0.060 ± 0.009	~ 25
Rat	0.038 ± 0.003	~ 75
Mouse	0.090	N/A

Figure 13

A.



B.

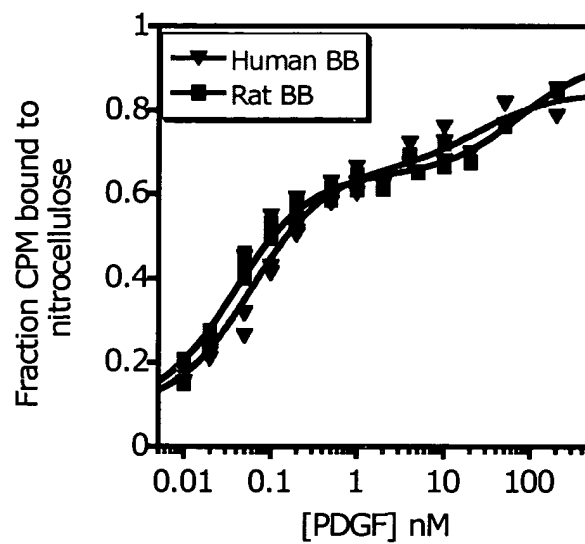
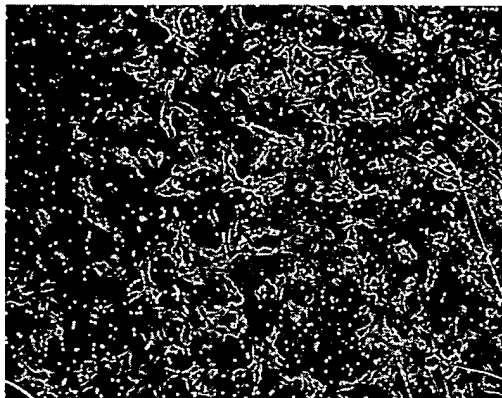
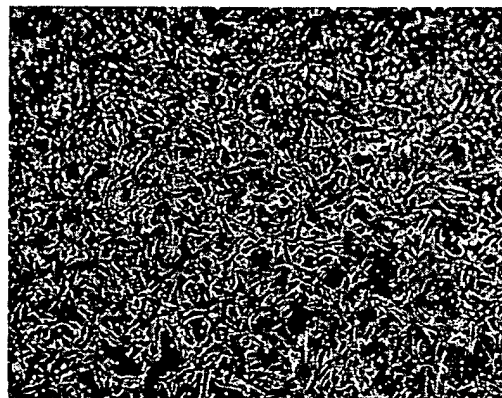


Figure 14

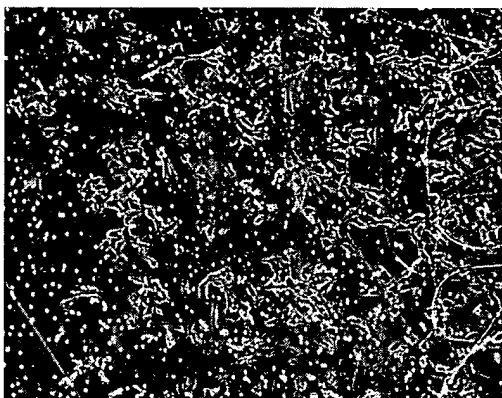
A.



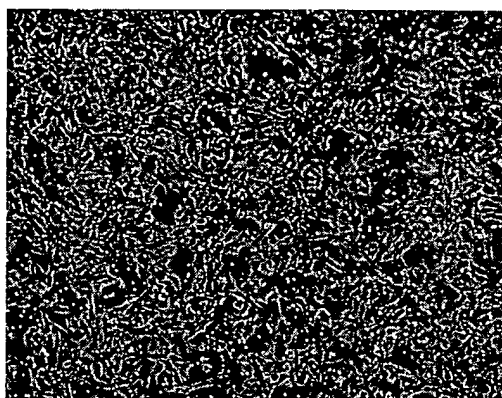
B.



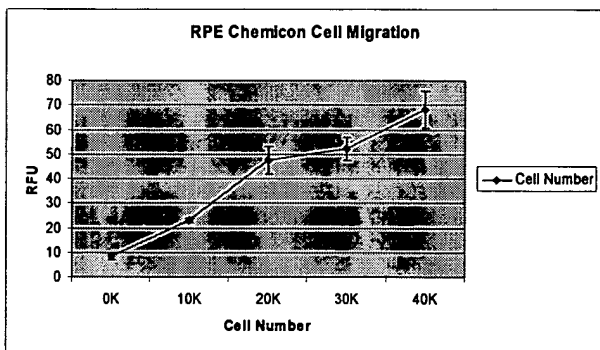
C.



D.



E.



F.

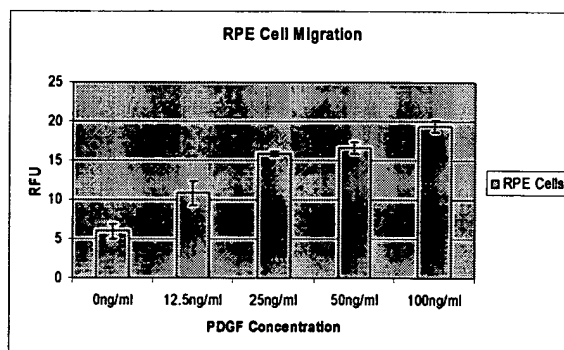


Figure 15

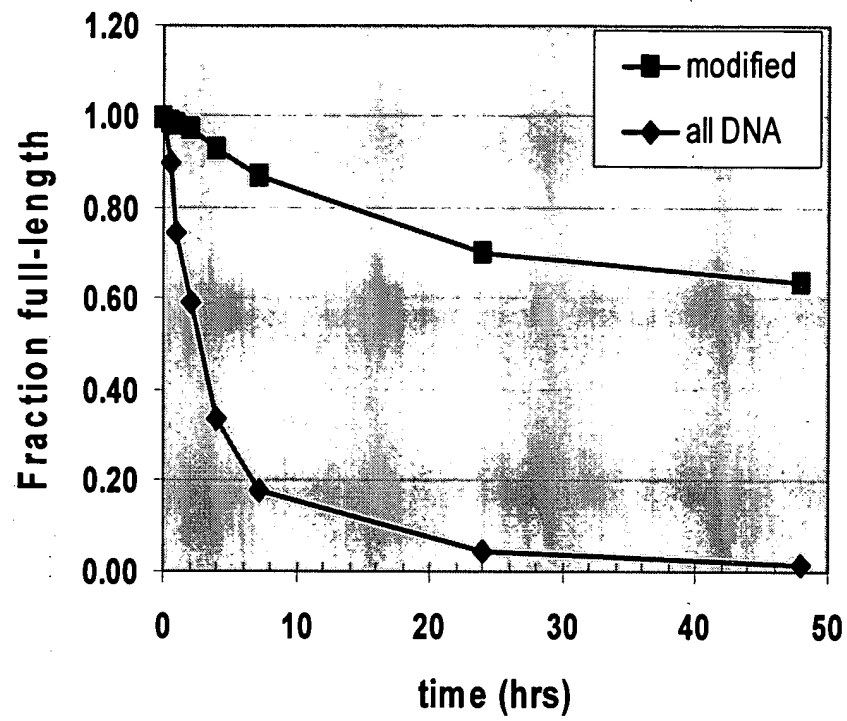


Figure 16

PK study 03002-002 - ARC127 IV, IP, SC admin, 10 mg/kg

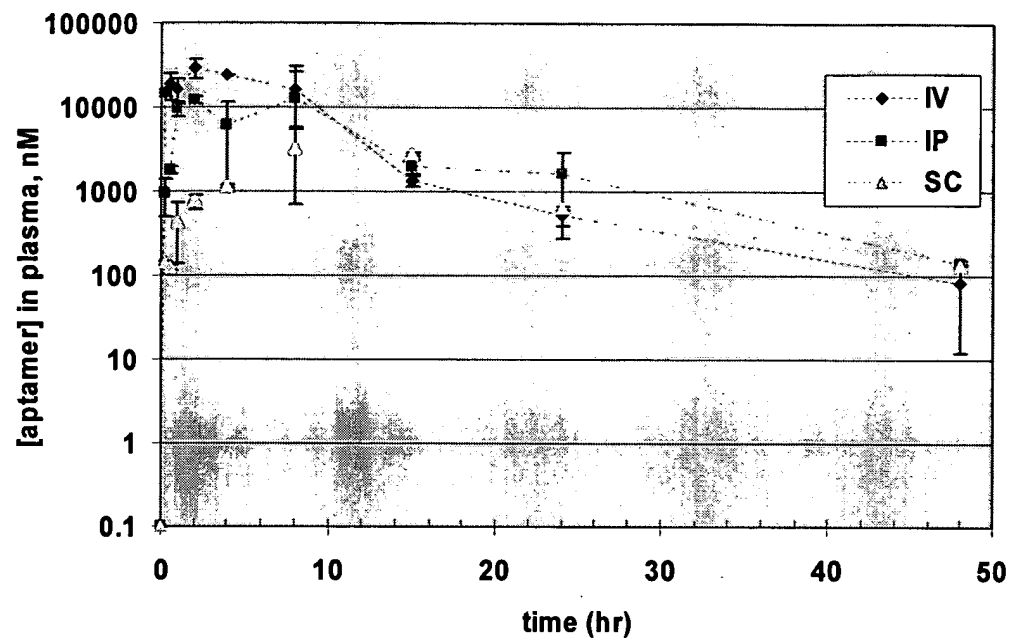


Figure 17

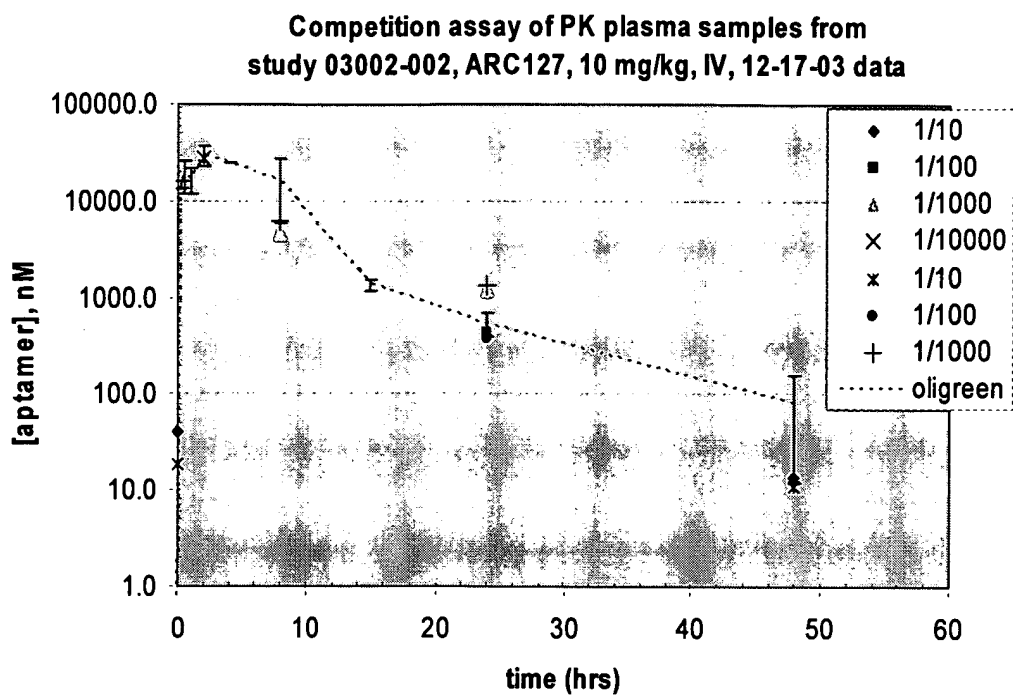
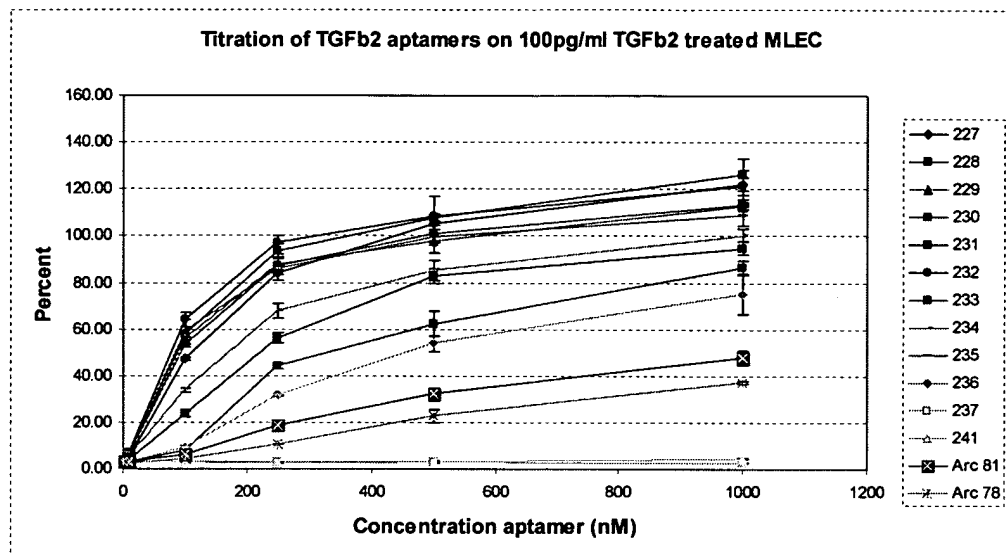


Figure 18

A.



B.

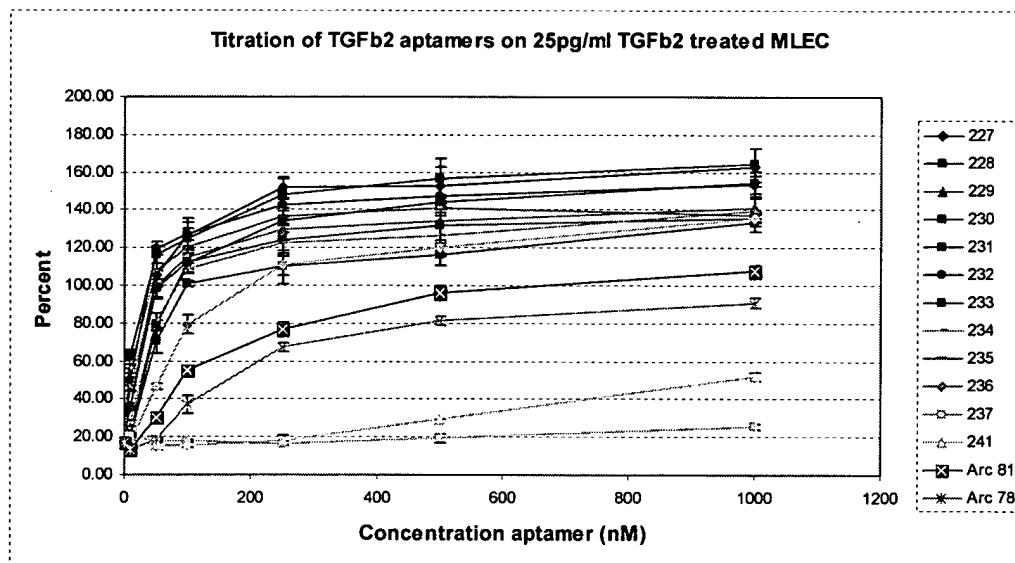
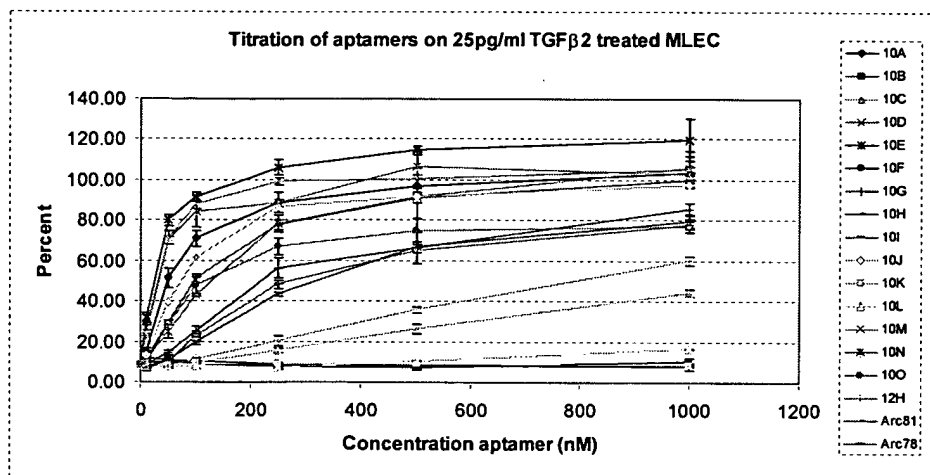
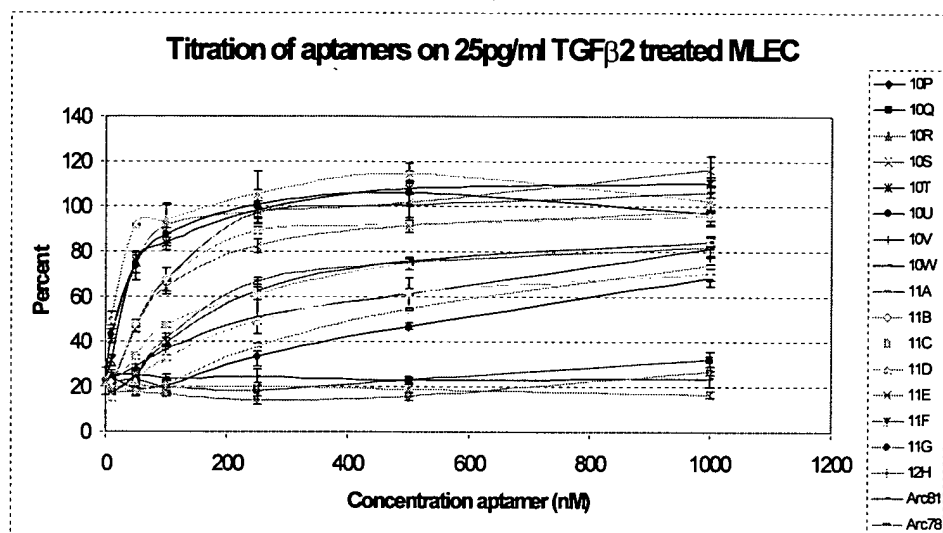


Figure 19

A.



B.



C.

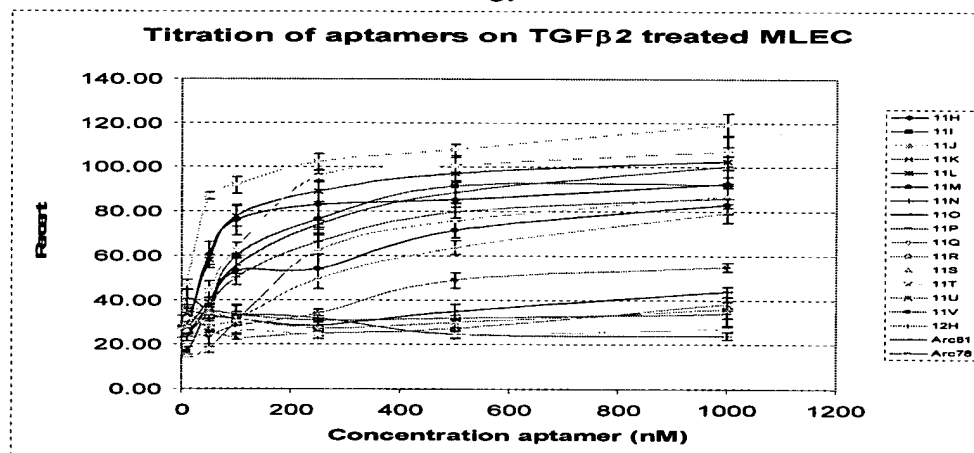
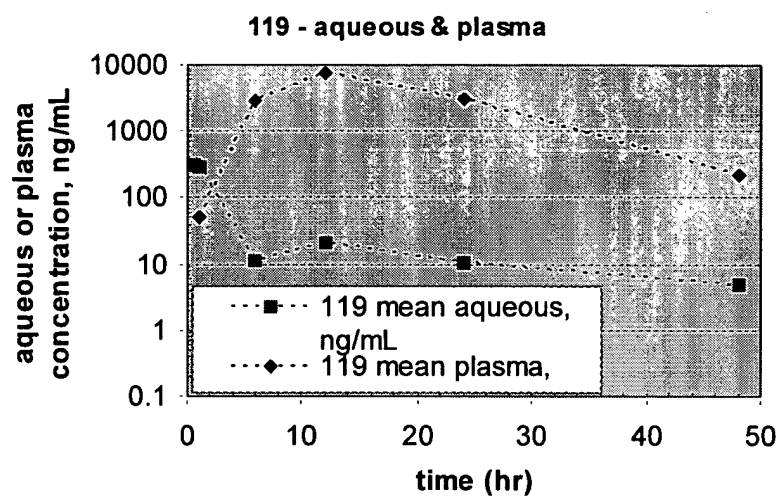


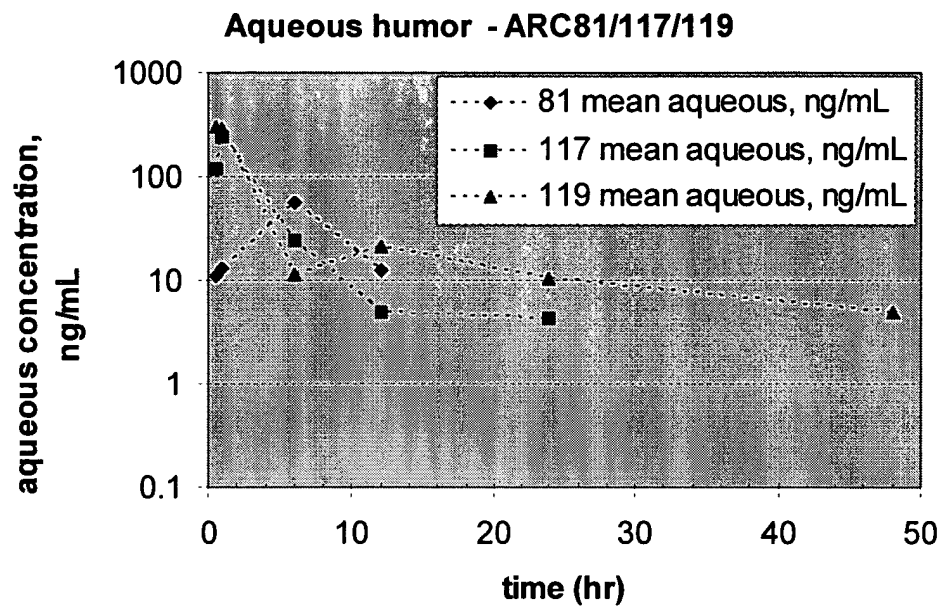
Figure 20

Figure 21A



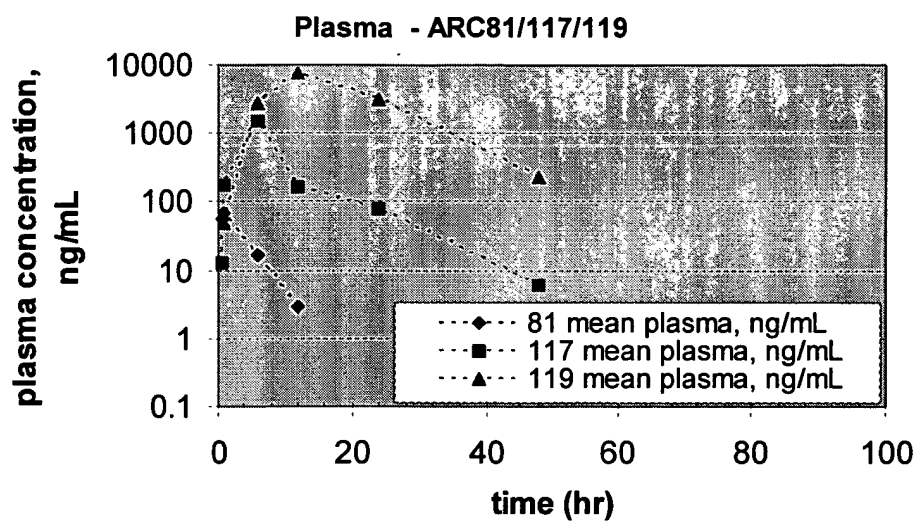
- subconj injection, 1 mg/eye, bilaterally
- $C_{max} (aq) = 303.8 \text{ ng/mL}$ (28.4 nM) at 0.5 hr
- $C_{max} (pl) = 7750.5 \text{ ng/mL}$ (721.1 nM) at 12 hr
- $MRT (aq) = 12.80 \text{ hr}$ ($t_{1/2} = 17.52 \text{ hr}$)
- $MRT (pl) = 17.28 \text{ hr}$ ($t_{1/2} = 6.94 \text{ hr}$)

Figure 21B



- subconj injection, 1 mg/eye, bilaterally
- MRT (81) = 6.03 hr (t_{\max} = 6 hr)
- MRT (117) = 3.62 hr (t_{\max} = 1 hr)
- MRT (119) = 12.80 hr (t_{\max} = 0.5 hr)

Figure 21C



- subconj injection, 1 mg/eye, bilaterally
- MRT (81) = 3.13 hr (t_{\max} = 1 hr)
- MRT (117) = 9.22 hr (t_{\max} = 6 hr)
- MRT (119) = 17.28 hr (t_{\max} = 12 hr)

Figure 22A

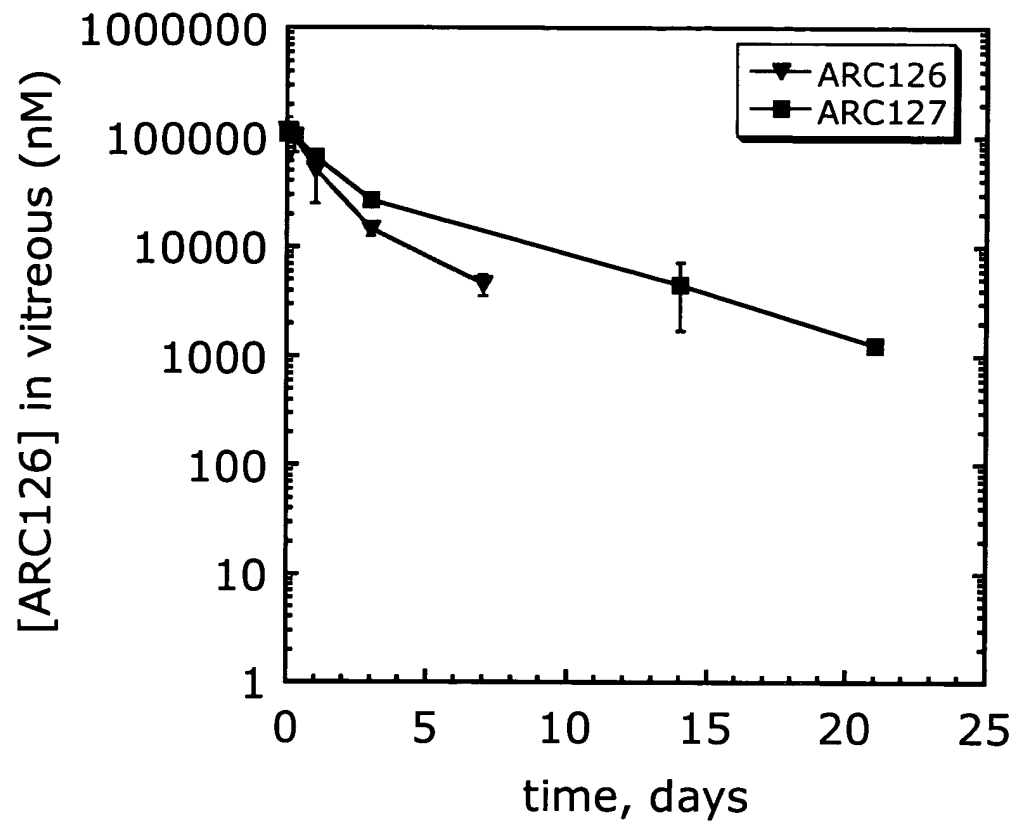


Figure 22B

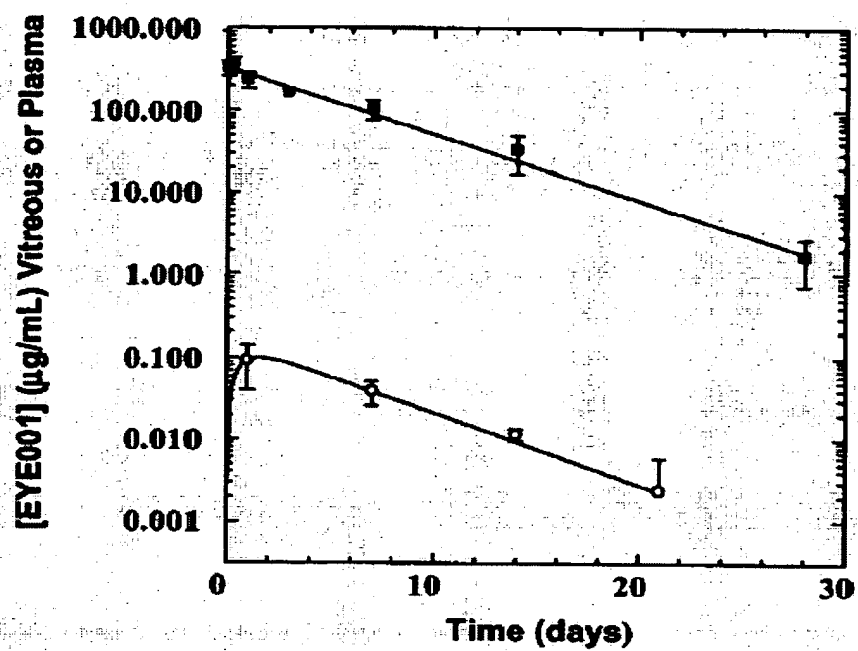


Figure 22C

